PARATHION AND ACUTE INTOXICATION. THE IMPORTANCE OF TOXICOLOGICAL ANALYTIC TESTS

Estela G. P. MARQUES, Maria M. OLIVEIRA, Paula V. MONSANTO, Paula PROENÇA, Fernando CASTANHEIRA, Duarte N. VIEIRA

Institute of Legal Medicine, University of Coimbra, Coimbra, Portugal

ABSTRACT: This paper describes the distribution of parathion in blood and various other organs, according to the etiology of the intoxication. As a rule, concentration levels are small, especially in the blood and in the stomach are higher, particularly in cases of suicide. In studies carried out on some patients admitted to hospital with parathion poisoning, entero-hepatic recirculation could have been a factor. We would stress the importance of all information in the interpretation of the results so as to arrive at a safe diagnosis.

KEY WORDS: Parathion; Interpretation of analytical results; Biological samples.

Problems of Forensic Sciences, vol. XLIII, 2000, 157–163
Received 9 September 1999; accepted 16 May 2000

INTRODUCTION

Organophosphate pesticides are the poisons that cause the greatest number of fatalities in the Central Region of Portugal. Among these, parathion, an organophosphate insecticide, is conspicuous for its high incidence [1, 4, 5, 8, 9, 10, 14, 16]. It presents an extremely acute toxicity for mammals. The lethal dose for man varies between 20 and 100 mg/kg body weight, and the admissible daily dose is 0.005 mg/kg body weight. It is a powerful cholinesterase inhibitor. Its most active metabolite (paraoxon) (Figure 1) is even more toxic. Parathion is rapidly absorbed through the gastro-intestinal tract and the skin, exhibits low bioavailability, binds readily to proteins and is easily eliminated, as experiments on animals, conducted by other researchers and by ourselves, have shown [12, 15]. This work is a synthesis of those data that we believe to be most important with respect to cases of poisoning by this insecticide.

Objective

It was our aim to underline the importance of general information, both clinical and circumstantial, as well as that of toxicological analyses of various biological materials taken from autopsies, in the interpretation of the analytical results, in order to determine the cause of death.

Fig. 1. Chemical structure of parathion and its metabolites.

Analytical methodology

Blood samples were performed following the method reported elsewhere [13] and the other biological samples were analysed using method B of our previously described procedure [11]. Analyses were performed using gas chromatography with a mass selective detector (GC/MS) by SIM (selective ion monitoring) mode, as well as using gas chromatography with nitrogen and phosphorus detection (GC/NPD).

Analytical-toxicological aspects

The concentrations of parathion in the different biological specimens of 230 intoxication cases performed in the Laboratory of Forensic Toxicology of the Institute of Legal Medicine of Coimbra, according their forensic etiology, are given in Table I. Blood was generally found to have the lowest concentrations, being lower than 0.01 μg/ml in 27% of cases. Therefore, other specimens should be analysed to gain a better understanding of the role of parathion in cases of intoxication. Stomach and/or gastric contents are very important, especially in cases of suicide, where enormous amounts are ingested. The parathion concentrations were higher than 1.0 μg/g in 73% of cases, and they usually smell of xylol and/or may have a milky appearance. In fatal human cases where there was no history (the subjects were found dead), with large amounts of parathion in the stomach, there were, as a rule, very small concentrations in most specimens examined (0.03 μg/ml or μg/g to 0.1 μg/g), with the exception of the small intestine, which agreed with our experimental study [15] in rabbits. In cases where the amounts absorbed exceed the lethal dose for rabbits, death takes at least 15 minutes and parathion is found in the different specimens in concentrations of 0.03 μg/ml or μg/g to

0.09 μg/ml or μg/g. Low levels of this insecticide are mainly found in the stomach and/or gastric contents, particularly due to consuming fruit, vegetables and water. We know that the maximum residual limits have been established for all products by the Portuguese Institute for the Protection of Agricultural Food Products (Instituto de Protecçno de Produçno Agro-Alimentar), but it is an unfortunate fact that farmers often fail to respect the established norms. Some researchers link depression cases among greenhouse workers to their moderate exposure levels (and occasionally high) of organophosphate insecticides. Parrón et al. [17] suggest that there may be a strong positive association between suicide and exposure to organophosphate insecticides, as consequence of a depressive episode before death. Analysis of the small intestine may be significant in cases when some time has elapsed between ingestion of the insecticide and the occurrence of death. Some results were positive with a cut-off of 1.0 μg/g.

TABLE I. DISTRIBUTION OF PARATHION IN THE DIFFERENT SPECIMENS ACCORDING TO ETIOLOGY [μg/ml; μg/g]

Material	n	Suicide X ± DP (range)	n	Homicide $\bar{X}$ ± DP (range)	n	Accident $\bar{X}$ ± DP (range)
Stomach	210	9832 ± 77225 (0–77232)	15	101.66 ± 102.66 (0.36–470)	16	19.16 ± 36.71 (0–105)
Blood	220	1.55 ± 2.0 (0–58)	13	0.64 ± 10.99 (0.004–23)	14	0.017 ± 0.026 (0–0.082)
Liver	200	5.0 ± 1578 (0.002–555)	12	0.66 ± 0.82 (0.003–1.12)	13	0.30 ± 0.62 (0.002–2.5)
Kidney	200	3.6 ± 450 (0–315)	10	0.16 ± 0.18 (0.026–0.39)	7	0.27 ± 0.43 (0.003–1.8)
Heart	52	7.1 ± 95 (1.0–32.7)		0.25 ± 0.31 (0.026–0.59)		
Small intestine	30	6.3 ± 462 (1.5–800.1)	6	5.80 ± 5.85 (0.78–10.2)		

In addition to blood, stomach and small intestine, other samples, such as liver, kidney and heart, were analysed and found to have higher average concentrations than in blood. There are two exceptions, kidney and heart samples in homicide cases, which present lower concentrations than those of blood samples.

Some of the fatal cases through ingestion of parathion had been admitted to hospital for treatment, during which body fluid samples were taken and analysed. The values found, though scarce, indicate that there may be an entero-hepatic recirculation (Figure 2).

There were four cases of parathion intoxication through dermal absorption. The average concentrations found in blood, liver and kidney samples were 0.031 μg/ml, 0.004 μg/g, and 0.003 μg/g respectively. The levels found in cases of dermal absorption t

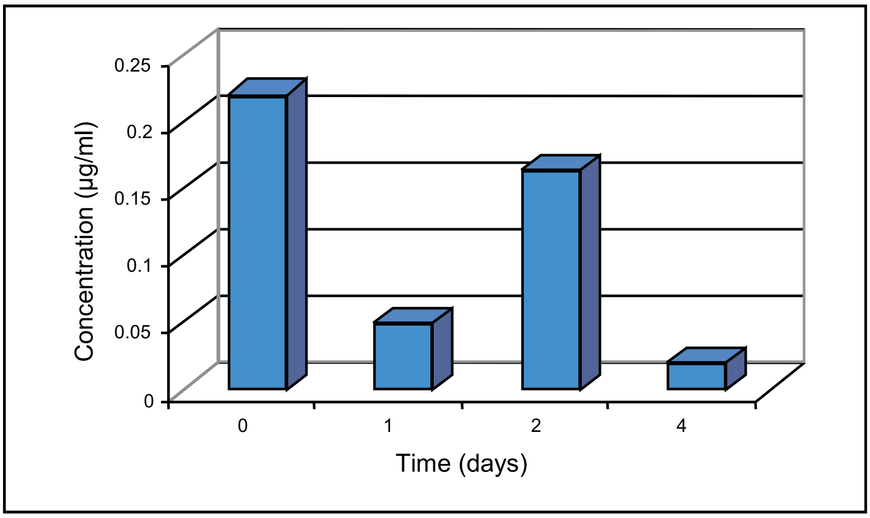

Fig. 2. Parathion concentrations in blood samples collected throughout the treatment in the hospital (n = 5).

hrough head skin tissues were much lower than those found in acute intoxications through ingestion, blood samples being those with higher concentration levels, contrary to what we observed in cases of acute intoxication through ingestion. According to Vale [19], the rate of parathion absorption varies according to the region of skin affected. It is absorbed more readily through scrotal skin, the armpits, and the skin of the head and neck than it is through the hands and arms. A study by Durham et al. [6] shows that the mean amount of liquid parathion absorbed through the skin was only 1.23% of the measured potential dermal exposure.

Paraoxon and aminoparathion metabolites were found in only a few cases. The p-nitrophenol and alkylphosphates (Figure 1) which can be detected in urine are not often analysed, since the bladder is usually empty in fatal cases. Some of the analytical findings are in agreement with those of other researchers [2, 3, 7, 18]. The analytical results were all negative eight days after absorption of the insecticide. Table II shows the partition coefficients (PC) between the specimens and blood samples. There was retention in the tissues (> 1.0) in the biological specimens tested, except in kidney samples in cases of homicide. It is noteworthy that the heart, which was analysed in cases of suicide only, had a higher PC value than those of other samples, with the exception of the small intestine, which shows higher values both in homicide and suicide cases. It should also be pointed out that the PC figures were even higher in cases of accidental intoxication.

TABLE II. PARTITION COEFFICIENTS BETWEEN THE SPECIMENS AND BLOOD SAMPLES

Material	n	Suicide PC	n	Homicide PC	n	Accident PC
Liver	200	3.7	10	1.3	12	14
Kidney	200	1.5	9	0.3	7	15
Heart	52	4.7	–	–	–	–
Small intestine	30	5.1	5	9.1	–	–

Some relevant considerations

The information given below facilitated post-mortem biological specimen tests and the interpretation of the results. The stomach and/or gastric contents were found to smell of xylol and/or have a milky appearance in 60% of cases. The small intestine was positive in 35% of cases, showing that there was some time elapsed between parathion ingestion and the death.

A previous analysis of the body fluids collected from patients admitted to the hospital was carried out in 15% of cases. There was medical assistance in 32% of cases, with the following typical clinical picture: muscarinic, nicotinic and neurologic syndromes and low cholinesterase levels. Complementary products found next to the victims were analysed in in 12% of the cases.

CONCLUSIONS

The relevant observations that we have mentioned above, as well as general information, help to choose the kind of analyses must be carried out and the interpretation of the results.

It should be noted that the analysis of the greatest possible number of specimens is of fundamental importance to the diagnosis, particularly in cases of accidental poisoning (usually where children are involved) and when the concentrations determined in most specimens are close to those found in farm workers or other persons, due to food and environmental contamination.

The anatomo-pathological findings are not specific to this kind of poisoning; there is only a general congestion of the organs, which is common to other cases of intoxication. Thus, the diagnosis of the cause of death can only be made through the analytical-toxicological results.

References:

1. Almeida L. M., Lima A. P., A propósito da intoxicação de uma criança pelo parathion, *O Médico* 1964, vol. 662, p. 3–20.
2. Beer J. de, Heyndrick A., Peteghem C. V., Suicidal poisoning by MCPA and Parathion, *Journal of Analytical Toxicology* 1980, vol. 4, pp. 91–98.
3. Chan L. T. F., Crowley R. J., Geyer R., Detection and analysis of aminoparathion in human post mortem specimens, *Journal of Forensic Sciences* 1983, vol. 28, pp. 122–127.
4. Costa R. B. C., Gomes J. D., Oliveira L. C., Rebelo M. A. T., Intoxicaçtes agudas por pesticidas. A propósito de 5 casos, *O Médico* 1969, vol. 54 , p. 210–216.
5. Costa R. B. C., Pimentel J. M., Gonçalves J. S., Rebelo A., Janeiro J., Prognostic factors in acute poisoning with organophosphorus pesticides – a study based on 190 cases, *Journal of Toxicology: Clinical Toxicology* 1985, vol. 23, pp. 448.
6. Durham W. F., Wolfe H. R., Elliott J. W., Absorption and excretion of parathion by spraymen, *Archives of Environmental Health* 1972, vol. 24, pp. 381–387.
7. Heyndrick A., Clerck F., Toxicological results and criteria of death, *J. Pharm. Belg.* 1977, vol. 32, pp. 149–161.
8. Lima A. P., Marques M. T. A., Intoxicação pelo parathion, *O Médico* 1962, vol. 576, p. 3–12.
9. Marques E. G. P., Determinação de pesticidas organofosforados em tecidos biológicos, II Jornadas Medico-Legal, Penafiel 1984 [oral comunication].
10. Marques E. G. P., Interpretação de resultados nas intoxicações por pesticidas organofosforados, I Congresso Ibérico de Medicina Legal, Funchal 1997 [oral comunication].
11. Marques E.G. P., Landeira A. C., Vieira D. N., Oliveira M. M. F., Monsanto P. C. V., Castanheira, A. M., Proença P., Methods for the quantification of parathion in tissues. A comparison between two clean-up procedures, 36th Annual Meeting of the International Association of Forensic Toxicologists, Albuquerque 1998.
12. Marques E. G. P., Monsanto P. V., Silva B. S., Vieira D. N., Ávila M. T., Oliveira M. M., Metabolism and toxicokinetic studies of parathion following oral administration in the rabbit, *Arquivos de Patologia Geral e Anatomia Patológica da Universidade de Coimbra* 1995, vol. XXVII, p. 65.
13. Marques E. G. P., Monsanto P. V., Silva B.S., Vieira D. N., Estudio comparativo de distintos metodos de extraccion del pesticida paration y sus metabolitos en fluidos biologicos, *Revista de Toxicologia* 1993, vol. 10, p. 99–100.
14. Marques E. G. P., Oliveira M. M., Landeira A. C., Silva B. S., Monsanto P. V., Intoxicaciones por paratión: estudio toxicologico 1983–1992, *Revista de Toxicologia* 1993, vol. 10, p. 94.
15. Marques E. G. P., Vieira D. N., Monsanto P. C. V., Silva B. P. S., Oliveira M. M. F., Castanheira A. M., Ávila M. T., Experimental studies with parathion insecticide in rabbits, 36th Annual Meeting of the International Association of Forensic Toxicologists, Albuquerque 1998.
16. Marques E.P., Oliveira M. M., Ávila M. T., Intoxicações mortais por pesticidas organofosforados, XXIII Jornadas Médicas da Figueira da Foz, Medicina do Trabalho 1988, p. 200–240.
17. Parrón T., Hernández A. F., Villanueva E., Increased risk of suicide with exposure to pesticides in an intensive agricultural area. A 12 year retrospective study, *Forensic Science International* 1996, vol. 79, pp. 53–63.

18. Tewari S.N., Harpalani S. P., Detection and determination of organophosphorus insecticides in tissues by thin-layer chromatography, *Journal of Chromatography* 1977, vol. 130, pp. 229–236.
19. Vale J.A., Toxicokinetic and toxicodynamic aspects of organophosphorus (OP) insecticide poisoning, *Toxicology Letters* 1998, vol. 102–103, pp. 649–652.